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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/527,525	10/14/2005	Athina Markou	TSRI 897.1	3218

26621 7590 05/03/2007

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1617	

MAIL DATE	DELIVERY MODE
05/03/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/527,525	MARKOU ET AL.	
	Examiner	Art Unit	
	Kendra D. Carter	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *10-15,17,19 and 23-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,16,18,20-22 and 27-31* is/are rejected.

7)☒ Claim(s) *16,18,22,28 and 31* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-31 are pending. Claims 10-15, 17, 19 and 23-26 are withdrawn.

Election/Restrictions

Applicant's election without traverse of Group I, claims 1-9, 16, 18, 20-22 and 27-31, in the reply filed on March 27, 2007 is acknowledged.

Specification

The disclosure is objected to because of the following informalities: the unit of the intensity is missing on page 69, line 1. Appropriate correction is required.

Claim Objections

(1) Claims 22, 28 and 31 are objected to because of the following informalities: the antagonist LY341495 should be stated as its formal name 2*S*-2-amino-2-(1*S*,2*S*-2-carboxycyclopropan-1-yl)-3-(xanth-9-yl)propionic acid), like the antagonist 2-methyl-6-(phenylethynyl)-pyridine (MPEP). Appropriate correction is required.

(2) Claims 16 and 18 are objected to because of the following informalities: the word "addictve" is misspelled. Appropriate correction is required.

Claim Rejections - 35 USC § 112 and 101

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 18 provides for the use of a combination according to any one of claims 10 to 13 for the preparation of a medicament for the treatment of an addictive disorder or depression, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 18 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

(1) Claims 1-4, 16, 18, 27 and 28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating a nicotine, alcohol, opiate, amphetamine, methamphetamine, or cocaine addiction, does not reasonably provide enablement for all metabotropic glutamate disorders and all addictive disorder. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to using the invention commensurate in scope with these claims.

The instant claims are drawn to a method of treating a metabotropic glutamate disorders wherein the disorder is an addictive disorder. The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention. Attention is directed to *In re Wands*, 8USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art;

(6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1) The nature of the invention:

The claim 1 is drawn to "a method for treating a metabotropic glutamate disorder, comprising administering to a subject in need thereof, an effective amount of at least one antagonist which modulates metabotropic glutamate receptor 3, and metabotropic glutamate receptor 5, thereby treating the disorder." The claim 4 is drawn to the "method of any one of claims 1 to 3, wherein the disorder is an addictive disorder." The claim 16 is drawn to a "method of treating a warm-blooded animal having an addictive disorder or depression comprising administering to the animal a combination according to any one of claims 10 to 13 in a quantity which is jointly therapeutically effective against an addictive disorder or depression and in which the compounds can also be present in the form of their pharmaceutically acceptable salts." The claim 27 is drawn to "a method for treating an addictive disorder, comprising: (a) administering to a subject in need thereof, an effective amount of at least one antagonist that modulates at least one of mGluR2,3, ad 5 during a first time period, wherein the first time period is a time period wherein the subject expects to be in an environment wherein, or exposed to stimuli in the presence of which, the subject habitually uses an addictive substance; and (b) administering at least one antagonist that modulates at least one of mGluR2 and/or 3 during a second time period, wherein the second time period is a time period wherein the subject is suffering from withdrawal and/or depression."

(2) The breadth of the claims:

Claims 1-4, 16, 18, 27 and 28 embraces and reads on treating all metabotropic glutamate disorders and/or all addictive disorders. The specification does not enable treating all metabotropic glutamate disorders and all addictive disorders.

(3) The state of the prior art:

The state of the art regarding treating all metabotropic glutamate disorders and all addictive disorders is very low or do not exist.

(4) The predictability or unpredictability of the art:

The predictability of all metabotropic glutamate disorders and all addictive disorders is relatively low. Therefore, to one skilled in the art, treating all metabotropic glutamate disorders and all addictive disorders is highly unpredictable.

(5) The relative skill of those in the art:

The relative skill of those in the art is high.

(6) The amount of direction or guidance presented / working examples:

In the instant case, the guidance of the specification as to the treating all metabotropic glutamate disorders and all addictive disorders is completely lacking. The specification as filed does not speak on or show any working examples any studies

performed that treat all metabotropic glutamate disorders and all addictive disorders. The specification gives examples of how to treat drug (i.e. nicotine, cocaine, and amphetamine) addictions on pages 32-124. Note that lack of a working example, is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art. See MPEP 2164.02.

(7) The quantity of experimentation necessary:

The instant claims read on treating all metabotropic glutamate disorders and all addictive disorders. As discussed above the specification fails to provide any support for treating all metabotropic glutamate disorders and all addictive disorders. Applicant fails to provide any information sufficient to practice the claimed invention, absent undue experimentation. For instance, one would need to perform tests in order to find all of the different disorders that the invention will treat. Additionally, one would need to test the invention to see if addictive disorders such as gambling, food, shopping and sexual disorders were treated with the invention. Both tests would require undue experimentation to practice the invention. Genetech, 108 F. 3d at 1366 states that " a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimation of general ideas that may or may not be workable.

In conclusion, the applicant is enabled for treating a nicotine, alcohol, opiate, amphetamine, methamphetamine, or cocaine addiction.

(2) Claims 8, 16, 18 and 29-31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating drug-induced depression and anxiety, does not reasonably provide enablement for treating non-drug induced depression and anxiety. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to using the invention commensurate in scope with these claims.

The instant claims are drawn to a method of treating depression. The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention. Attention is directed to *In re Wands*, 8USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1) The nature of the invention:

The claim 1 is drawn to "a method for treating a metabotropic glutamate disorder, comprising administering to a subject in need thereof, an effective amount of at least one antagonist which modulates metabotropic glutamate receptor 3, and metabotropic glutamate receptor 5, thereby treating the disorder." The claim 8 is drawn to the "method of any one of claims 1 to 3, wherein the disorder is depression." The claim 16 is drawn to a "method of treating a warm-blooded animal having an addictive disorder or depression comprising administering to the animal a combination according to any one of claims 10 to 13 in a quantity which is jointly therapeutically effective against an addictive disorder or depression and in which the compounds can also be present in the form of their pharmaceutically acceptable salts." The claim 18 is drawn to a "use of a combination according to any one of claims 10 to 13 for the preparation of a medicament for the treatment of an addictive disorder or depression." The claim 29 is drawn to "a method for treating depressive symptoms and anxiety symptoms of depression, comprising administering to a subject in need thereof, and effective amount of at least one antagonist that modulates metabotropic glutamate receptor 2, metabotropic glutamate receptor 3, and metabotropic glutamate receptor 5, thereby treating the depressive symptoms and anxiety symptoms of depression."

(2) The breadth of the claims:

Claims 8, 16, 18 and 29-31 embrace and read on treating depression or/and anxiety symptoms of depression. The specification does not enable treating non-drug induced depression or/and anxiety symptoms of depression.

(3) The state of the prior art:

The state of the art regarding treating depression is high.

(4) The predictability or unpredictability of the art:

The predictability of treating depression or/and anxiety symptoms of depression by administering an effective amount of at least one antagonist which modulates metabotropic glutamate receptor 2, and/or metabotropic glutamate receptor 3, and/or metabotropic glutamate receptor 5 is relatively low. Therefore, to one skilled in the art, treating depression or/and anxiety symptoms of depression by administering an effective amount of at least one antagonist which modulates metabotropic glutamate receptor 2, and/or metabotropic glutamate receptor 3, and/or metabotropic glutamate receptor 5 is highly unpredictable.

(5) The relative skill of those in the art:

The relative skill of those in the art is high.

(6) The amount of direction or guidance presented / working examples:

In the instant case, the guidance of the specification as to the treating depression or/and anxiety symptoms of depression by administering an effective amount of at least one antagonist which modulates metabotropic glutamate receptor 2, and/or metabotropic glutamate receptor 3, and/or metabotropic glutamate receptor 5 is

completely lacking. The specification as filed does not speak on or show any working examples any studies performed that treat depression or/and anxiety symptoms of depression that is not induced by a drug addiction. The specification gives examples of how to treat drug-induced depression (see page 79, paragraph 2, lines 1 and 2), but states that the treatment "may be effective to treat non-drug-induced depression also" (see page 79, paragraph 2, last two lines) and "MPEP may block the mildly heightened anxiety levels induced by nicotine" (see page 61, paragraph 1, last 3 line). It is noted that anxiety is known to be a major symptom of the overall syndrome of depression (see page 21, paragraph 1, last 3 lines). Note that lack of a working example, is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art. See MPEP 2164.02.

(7) The quantity of experimentation necessary:

The instant claims read on treating depression or/and anxiety symptoms of depression. As discussed above the specification fails to provide any support for treating depression that is not induced by a drug addiction. Applicant fails to provide any information sufficient to practice the claimed invention, absent undue experimentation. For instance, there are several forms of depression that are not associated with drug addiction such as post-partum depression and long-term depression. One would need to perform tests to see if the invention treated such patients effectively, because the guidance the specification only states that the treatment may be effective. Genetech, 108 F. 3d at 1366 states that " a patent is not a

hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimation of general ideas that may or may not be workable.

In conclusion, the applicant is enabled for treating drug-induced depression or/and anxiety symptoms of depression.

(3) Claims 1-8, 16, 18, 20, 21, 27, 29 and 30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for administering the antagonists LY341495, p-MPPI, 2-methyl-6-(phenylethynyl)-pyridine (MPEP), (+)-MK-801, LY341495, NBQX disodium, LY314582, and LY354740, does not reasonably provide enablement for all metabotropic glutamate receptor 2, and/or metabotropic glutamate receptor 3, and/or metabotropic glutamate receptor 5 antagonist. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant claims are drawn to a method wherein an effective amount of a metabotropic glutamate receptor 2, and/or metabotropic glutamate receptor 3, and/or metabotropic glutamate receptor 5 antagonist is administered. The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention. Attention is directed to *In re Wands*, 8USPQ2d 1400 (CAFC 1988) at 1404

where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1) The nature of the invention:

The claim 1 is drawn to "a method for treating a metabotropic glutamate disorder, comprising administering to a subject in need thereof, an effective amount of at least one antagonist which modulates metabotropic glutamate receptor 3, and metabotropic glutamate receptor 5, thereby treating the disorder." The claim 16 is drawn to a "method of treating a warm-blooded animal having an addictive disorder or depression comprising administering to the animal a combination according to any one of claims 10 to 13 in a quantity which is jointly therapeutically effective against an addictive disorder or depression and in which the compounds can also be present in the form of their pharmaceutically acceptable salts." The claim 18 is drawn to a "use of a combination according to any one of claims 10 to 13 for the preparation of a medicament for the treatment of an addictive disorder or depression." The claim 20 is drawn to "a method for treating substance abuse, comprising administering to a subject in need thereof, an effective amount of at least one antagonist which modulates mGluR2, mGluR3, and

mGluR5, or a combination according to any one of claims 10 to 13, wherein the effective amount is sufficient to diminish, inhibit or eliminate desire for and/or consumption of the substance in the subject." The claim 27 is drawn to "a method for treating an addictive disorder, comprising: (a) administering to a subject in need thereof, an effective amount of at least one antagonist that modulates at least one of mGluR2, 3, and 5 during a first time period, wherein the first time period is a time period wherein the subject expects to be in an environment wherein or exposed to stimuli in the presence of which, the subject habitually uses an addictive substance; and (b) administering at least one antagonist that modulates at least one of mGluR2 and/or 3 during a second time period, wherein the second time period is a time period wherein the subject is suffering from withdrawal and/or depression." The claim 29 is drawn to "a method for treating depressive symptoms and anxiety symptoms of depression, comprising administering to a subject in need thereof, and effective amount of at least one antagonist that modulates metabotropic glutamate receptor 2, metabotropic glutamate receptor 3, and metabotropic glutamate receptor 5, thereby treating the depressive symptoms and anxiety symptoms of depression."

(2) The breadth of the claims:

Claims 1-8, 16, 18, 20, 21, 27, 29 and 30 embrace and read on a method wherein an effective amount of a metabotropic glutamate receptor 2, and/or metabotropic glutamate receptor 3, and/or metabotropic glutamate receptor 5 antagonist is administered. The specification does not enable administering all or any

metabotropic glutamate receptor 2, and/or metabotropic glutamate receptor 3, and/or metabotropic glutamate receptor 5 antagonist.

(3) The state of the prior art:

The state of the art regarding a method wherein an effective amount of all or any metabotropic glutamate receptor 2, and/or metabotropic glutamate receptor 3, and/or metabotropic glutamate receptor 5 antagonist is administered to treat a metabotropic glutamate disorder or/and an addictive disorder, or/and depression or/and anxiety symptoms of depression is very low or do not exist. .

(4) The predictability or unpredictability of the art:

The predictability of administering an effective amount of all or any metabotropic glutamate receptor 2, and/or metabotropic glutamate receptor 3, and/or metabotropic glutamate receptor 5 antagonist is administered to treat a metabotropic glutamate disorder or/and an addictive disorder, or/and depression or/and anxiety symptoms of depression is relatively low. Therefore, to one skilled in the art, administering an effective amount of all or any metabotropic glutamate receptor 2, and/or metabotropic glutamate receptor 3, and/or metabotropic glutamate receptor 5 antagonist is administered to treat a metabotropic glutamate disorder or/and an addictive disorder, or/and depression or/and anxiety symptoms of depression is highly unpredictable.

(5) The relative skill of those in the art:

The relative skill of those in the art is high.

(6) The amount of direction or guidance presented / working examples:

In the instant case, the guidance of the specification as to administering an effective amount of all or any metabotropic glutamate receptor 2, and/or metabotropic glutamate receptor 3, and/or metabotropic glutamate receptor 5 antagonist is administered to treat a metabotropic glutamate disorder or/and an addictive disorder, or/and depression or/and anxiety symptoms of depression is completely lacking. The specification as filed does not speak on or show any working examples any studies performed that administer an effective amount of all or any metabotropic glutamate receptor 2, and/or metabotropic glutamate receptor 3, and/or metabotropic glutamate receptor 5 antagonist is administered to treat a metabotropic glutamate disorder or/and an addictive disorder, or/and depression or/and anxiety symptoms of depression. The specification gives examples administering effective amount of LY341495, p-MPPI, 2-methyl-6-(phenylethynyl)-pyridine (MPEP), (+)-MK-801, LY341495, NBQX disodium, LY314582, and LY354740 to treat a nicotine, alcohol, opiate, amphetamine, methamphetamine, or cocaine addiction, or/and a drug-induced depression or/and anxiety symptoms of depression (see examples pages 34-124). Note that lack of a working example, is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art. See MPEP 2164.02.

(7) The quantity of experimentation necessary:

The instant claims read on treating depression or/and anxiety symptoms of depression. As discussed above the specification fails to provide any support for treating depression that is not induced by a drug addiction. Applicant fails to provide any information sufficient to practice the claimed invention, absent undue experimentation. Although some mGluR 2, 3, and/or 5 antagonist are known in the art, there are some that are not. The anatagonist that are not known, one would need to perform test to see if the compounds are antagonist of mGluR 2, 3, and/or 5. Second, for those that are known mGluR 2, 3, and/or 5 antagonist one would need to perform test to see which ones were effective and there amounts to combine to treat a nicotine, alcohol, opiate, amphetamine, methamphetamine, or cocaine addiction, or/and a drug-induced depression or/and anxiety symptoms of depression. These tests require undue experimentation. Genetech, 108 F. 3d at 1366 states that " a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimation of general ideas that may or may not be workable.

In conclusion, the applicant is enabled for administering the antagonists LY341495, 2-methyl-6-(phenylethynyl)-pyridine (MPEP), (+)-MK-801, LY341495, NBQX disodium, LY314582, and LY354740.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

(1) Claims 1-5, 20 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Fundytus et al. (British Journal of Pharmacology, 1997, vol. 120, pp. 1015-1020).

Fundytus et. al. teaches a method of treating morphine withdrawal symptoms by administering an effective amount of the mGluR 1, 2, 3, and 5 antagonist α-methyl-4-carboxyphenylglycine (MCPG); see abstract paragraph 1, paragraph 2, lines 7 and 8. Also, The mGluR 2 and 3 antagonist 2S, 1'S, 2'S-2-methyl-2-(2'-carboxycyclopropyl) glycine (MCCG) and the mGluR 4, 6, 7 and 8 antagonist α-methyl-L-amino-4-phosphonobutanoate (MAP4) also treated withdrawal symptoms (see abstract, paragraph 2, lines 2-6 and paragraph 3).

(2) Claims 1-5, 7, 9, 20 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Chiamulera et al. (Nature Neuroscience, 2001, vol. 4(9), pp. 873-874).

Chiamulera et al. teaches the significant contribution of mGlu5 receptors to the behavioral effects of cocaine addiction (see page 873, column 1, paragraph 1, last 4 lines). A decrease of self-administration of cocaine was observed with an administration of the mGluR5 antagonist 2-methyl-6-(phenylethynyl)-pyridine (MPEP); see page 873, column 2, last paragraph, lines 1-4).

(3) Claims 1-8, 20, 21 and 29 are rejected under 35 U.S.C. 102(b) as being anticipated by Adam et al. (US 6407,094 B1).

Adam et al. teaches compounds that act as Group II (i.e. mGluR 2 and 3) metaboltropic glutamate receptor antagonist (see column 16, lines 47 and 48) and treat conditions which lead to glutamate-deficiency functions such as nicotine addiction, opiate addiction, anxiety and depression (see column 1, lines 54-56 and column 3, lines 20-24). In regards to the compounds specifically antagonizing mGluR 2,3, and/or 5, this is an inherent property of treating the nicotine addiction, opiate addiction, anxiety and depression. The antagonist can be in their pharmaceutically acceptable salts (see column 3, line 4).

(3) Claims 1-8, 20, 21 and 29 are rejected under 35 U.S.C. 102(e) as being anticipated by Corsi et al. (US 2003/0195139 A1).

Corsi et al. teaches a method of treating substance dependence, wherein the substance is nicotine, opiate, cocaine, amphetamine, benzodiazepine and ethanol, comprising administering a therapeutically effective amount of an antagonist of mGluR5 (see claims 21-23). Depression and anxiety is also treated (see page 7, paragraph 119, line 7). The compounds can be in the form of salts (see page 3, paragraph 55, lines 1 and 2). In regards to the compounds specifically antagonizing mGluR 2,3, and 5, this is an inherent property of treating the substance dependence, anxiety and depression.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

(1) Claims 16, 18 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Adam et al. (US 6407,094 B1) as applied to claims 1-8, 20 and 21 above in view of Corsi et al. (US 2003/0195139 A1) as applied to claims 1-8, 20, 21 and 29 above.

Adam et al. teachings are as applied to claims 1-8, 20 and 21 above.

Corsi et al. teachings are as applied to claims 1-8, 21 and 29 above.

Adam et al. and Corsi et al. does not teach a combination according to any one of claims 10 to 13.

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the method of Adam et al. and a combination according to any one of claims 10 to 13 because of the following: (1) both Adam et al. and Corsi et al. teach methods that treat addictive disorders or depression; (2) Adam et al. teaches the treatment of addictive disorders or depression with a mGluR 2 and 3 antagonist; and (3) Corsi et al. teaches the treatment of an addictive disorder or depression with a mGluR 5 antagonist. One would be motivated to combine the two methods because although different compounds are used and antagonize different mGluR's, they both treat addictive disorders or depression. "It is *prima facie* obvious to

combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). See also *In re Crockett*, 279 F.2d 274, 126 USPQ 186 (CCPA 1960); *Ex parte Quadranti*, 25 USPQ2d 1071 (Bd. Pat. App. & Inter. 1992); and *In re Geiger*, 815 F.2d 686, 2 USPQ2d 1276 (Fed. Cir. 1987).

(2) Claim 22, 27 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chiamulera et al. (Nature Neuroscience, 2001, vol. 4(9), pp. 873-874) as applied to claims 1-5, 7, 9, 20 and 21 above in view of Adam et al. (US 6407,094 B1).

Chiamulera et al. teachings are as applied to claims 1-5, 7, 9, 20 and 21 above.

Chiamulera et al. does not teach the antagonist LY341495, nor the combination according to any one of claims 10 to 13. Also, the administration comprising: (a) administering to a subject in need thereof, an effective amount of at least one antagonist that modulates at least one of mGluR2, 3, and 5 (specifically LY341495 or/and MPEP) during a first time period, wherein the first time period is a time period wherein the subject expects to be in an environment wherein or exposed to stimuli in the presence of which, the subject habitually uses an addictive substance; and (b)

administering at least one antagonist that modulates at least one of mGluR2 and/or 3 (specifically LY341495) during a second time period, wherein the second time period is a time period wherein the subject is suffering from withdrawal and/or depression, is not taught.

Adam et al. teaches compounds that act as Group II (i.e. mGluR 2 and 3) metaboltropic glutamate receptor antagonist (see column 16, lines 47 and 48) and treat conditions which lead to glutamate-deficiency functions such as nicotine addiction, opiate addiction, anxiety and depression (see column 1, lines 54-56 and column 3, lines 20-24). In regards to the compounds specifically antagonizing mGluR 2,3, and/or 5, this is an inherent property of treating the nicotine addiction, opiate addiction, anxiety and depression.

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the method of Chiamulera et al. and the antagonist LY341495 because of the following: (1) both Chiamulera et. al. and Adam et al. teach methods to treat substance abuse; (2) Adam et al. teaches the treatment of an addictive disorders or depression with a mGluR 2 and 3 antagonist; and (3) LY341495 is a well known mGluR 2 and 3 antagonist in the art (indicated by the specification page 14, paragraph 2, lines 1 and 2, and page 16, group II, line 1 and 4). One would be motivated to combine the two methods because although different compounds are used and antagonize different mGluR's, they both treat substance abuse. "It is *prima facie*

obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). See also *In re Crockett*, 279 F.2d 274, 126 USPQ 186 (CCPA 1960); *Ex parte Quadranti*, 25 USPQ2d 1071 (Bd. Pat. App. & Inter. 1992); and *In re Geiger*, 815 F.2d 686, 2 USPQ2d 1276 (Fed. Cir. 1987).

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the method of Chiamulera et al. and an administration comprising: (a) administering to a subject in need thereof, an effective amount of at least one antagonist that modulates at least one of mGluR2, 3, and 5 (specifically LY341495 or/and MPEP) during a first time period, wherein the first time period is a time period wherein the subject expects to be in an environment wherein or exposed to stimuli in the presence of which, the subject habitually uses an addictive substance; and (b) administering at least one antagonist that modulates at least one of mGluR2 and/or 3 (specifically LY341495) during a second time period, wherein the second time period is a time period wherein the subject is suffering from withdrawal and/or depression; because without unexpected results, one skilled in the art can reasonably design the period of administration.

(3) Claims 30 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bear et al. (US 6,916,821 B2) in view of Adam et al. (US 6407,094 B1).

Bear et al. teaches a method of treating anxiety comprising administering an effective amount of the Group I mGluR antagonist (i.e. mGluR 1 and 5), MPEP (see claims 1 and 2).

Bear et al. does not teach the antagonist LY341495. Also, a method wherein an antagonist of metabotropic glutamate receptor 2 and metabotropic glutamate receptor 3 (specifically LY341495) is administered when the subject experiences depression symptoms, and an antagonist of metabotropic glutamate receptor 5 (specifically MPEP) is administered when the subject experiences anxiety symptoms is not taught.

Adam et al. teaches compounds that act as Group II (i.e. mGluR 2 and 3) metaboltropic glutamate receptor antagonist (see column 16, lines 47 and 48) and treat conditions which lead to glutamate-deficiency functions such as nicotine addiction, opiate addiction, anxiety and depression (see column 1, lines 54-56 and column 3, lines 20-24). In regards to the compounds specifically antagonizing mGluR 2,3, and/or 5, this is an inherent property of treating the nicotine addiction, opiate addiction, anxiety and depression.

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the method of Bear et al. and the antagonist LY341495 because of the following: (1) Bear et al. teaches a method of treating anxiety with the mGluR 5 antagonist MPEP; (2) Adam et al. teaches a method of treating depression and anxiety with a mGluR 2 and 3 antagonist; and (3) LY341495 is a well known mGluR 2 and 3 antagonist in the art (indicated by the specification page 14, paragraph 2, lines 1 and 2, and page 16, group II, line 1 and 4). One would be motivated to combine the two methods because although different compounds are used and antagonize different mGluR's, they both treat addictive disorders or depression. "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). See also *In re Crockett*, 279 F.2d 274, 126 USPQ 186 (CCPA 1960); *Ex parte Quadranti*, 25 USPQ2d 1071 (Bd. Pat. App. & Inter. 1992); and *In re Geiger*, 815 F.2d 686, 2 USPQ2d 1276 (Fed. Cir. 1987).

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the method of Chiamulera et al. and an administration comprising: an antagonist of metabotropic glutamate receptor 2 and metabotropic glutamate receptor 3 administered when the subject experiences depression symptoms, and an antagonist of metabotropic glutamate receptor 5

administered when the subject experiences anxiety symptoms, because without unexpected results, one skilled in the art can reasonably design the period of administration.

Conclusion

No claims are allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kendra D. Carter whose telephone number is (571) 272-9034. The examiner can normally be reached on 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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KDC

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